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ORIGINAL ARTICLE – OPEN ACCESS

Clinical Significance of Incidental 18-FDG Uptake in Nasopharynx on PET/CT Scanning

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ABSTRACT

Objective: The necessity of biopsy in cases of incidental nasopharyngeal 18 fluorodeoxyglucose (18-FDG) uptake was investigated in this study.

Materials and Methods: A total of 27 patients, who suffered incidental 18-FDG uptake in their nasopharynx, were enrolled in the study. Their primary malignant diseases, physical examination findings, standardized uptake values (SUV), uptake sides, and nasopharynx biopsy results were evaluated.

Results: There were 23 benign and 4 malignant tumors found on the biopsy results. A total of 10 patients had visible lesions in their physical examinations. When the data were evaluated statistically, the relationship between the visible lesion and the nasopharyngeal biopsy results was found to be significant ($p<0.05$). All the patients who had a malignant biopsy result also had a history of lymphoma and an asymmetrical nasopharyngeal uptake. There was no significant difference between the SUVmax value and the biopsy result.

Conclusion: Biopsy can be considered in patients who have a visible lesion in the nasopharynx examination, a history of lymphoma, and asymmetrical nasopharyngeal uptake according to the PET scan.

Keywords: Lymphoma, SUVmax, endoscopy

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INTRODUCTION

The 18 Fluorodeoxyglucose Positron Emission Tomography (FDG PET) test is a common and successful diagnostic method with a working principle of increasing the activity in malignant cells (1, 2). The increased activity is not specific to malignancies and can be seen in infectious, inflammatory, and benign conditions as well (3). In head and neck area, FDG uptake by normal tissues, such as salivary glands, vocal folds, and the lymphoid tissue in the Waldeyer ring may give false-positive results (4).

Patients with incidental FDG uptake in the nasopharynx in their PET scans, who have cancer in sites other than the nasopharynx, are directed to otolaryngology clinics. The question of whether biopsy is required for all patients remains unanswered, since performing biopsy in every patient is not only painful but also costly. The aim of this study was to evaluate the necessity of nasopharynx biopsy in patients with incidental PET activity.

MATERIALS and METHODS

After obtaining the ethical committee approval (Decision number: 2014/358), 27 patients with incidental nasopharyngeal FDG uptake in their PET scans between January 2014 and September 2014 were included in the study. Patients who had a history of nasopharyngeal cancer were excluded. Patient information was examined and recorded retrospectively. All the patients received a head-neck physical examination. Primary diseases, ear examination findings, endoscopic examinations, standardized uptake values (SUV), and features of uptake patterns (symmetric or asymmetric) were listed. Nasopharyngeal biopsy of suspicious areas was performed for every patient by an experienced head and neck surgeon. When there was no suspicious area, the biopsy was done from the metabolically active area in the PET scan. There were no patients with serous otitis media or fluid accumulation in the middle ear. There were 10 patients who had visible lesions in their endoscopic examination. There were 11 patients with symmetrical uptake and 16 patients with asymmetrical uptake in the PET scan. The nasopharyngeal biopsy results, patients' clinical features, and PET findings were compared.

PET Imaging: PET-CT imaging was done using a combined whole-body PET/CT in-line system (Gemini TF PET/CT scanner, Philips Medical Systems, Cleveland, Ohio, U.S.A) equipped with a high-resolution PET scanner and a 16-slice Briliance CT machine. Patients were informed to fast for at least 6 hours prior to the procedure. Then blood glucose level was obtained before the injection of the tracer. Based on each patient's body weight, approxi-

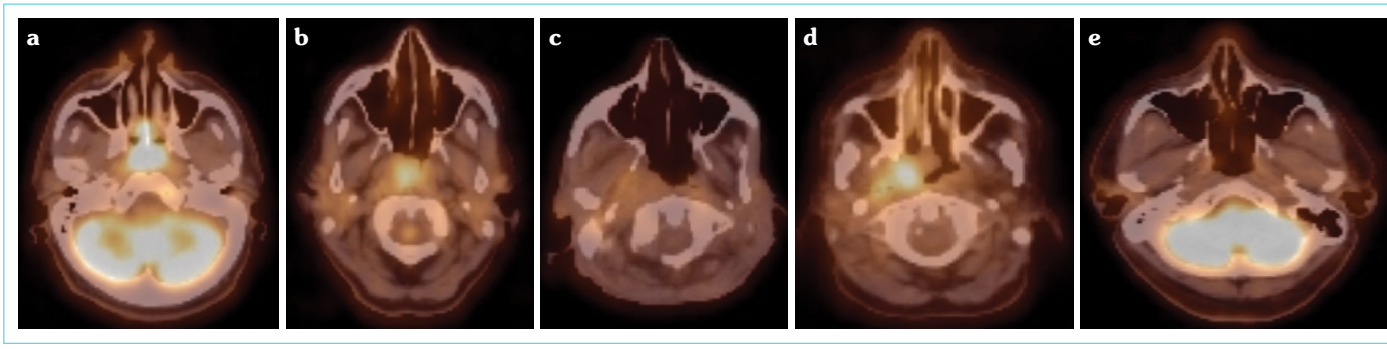

Figure 1. a–e. PET/CT samplesof some conditions on nasopharynx. (a) Nasopharynx cancer. (b) Nasopharyngeal uptake of Hodgkin's lymphoma. (c) Nasopharyngeal uptake of T cell lymphoma. (d) Verrucous hyperplasia. (e) Psysiologic uptake

mately 222-444 MBq (6–12 mCi) of F-18 FDG was injected. Scanning was started 60 minutes after the intravenous injection of F-18 FDG as a bolus. Initially, either a low-dose supine CT scan (140 kVp, 80 mA, transaxial FOV: 600 mm, Pitch: 1.1, slice thickness: 5 mm) from the base of the skull to the mid-thighs or a whole-body scan without any contrast agent was acquired for attenuation correction. Afterwards, a high-resolution supine PET dataset (axial full-width at half-maximum 8 mm) over the same region was obtained in 5–8 bed positions with an obtaining time of 1 minute for each bed position. The PET images were reconstructed using iterative reconstruction with a CT-derived decline correction using the ordered subsets expectation maximization algorithm. PET, CT, and fused PET/CT images were evaluated in multiplanar reconstructions using the software developed by the producer (Extended Brilliance Workstation, Philips Medical System).

All PET/CT images were evaluated by two physicians who with rich experience in nuclear medicine. Focal accumulation of FDG above the background (liver, non-working muscle) was considered as a positive finding. For a qualitative evaluation, the non-attenuation-corrected FDG-PET images, as well as the attenuation-corrected FDG-PET/CT images, were evaluated on maximum density projection images for each patient to assess the presence or absence of elevated tracer uptake. In addition to qualitative evaluation of the images, both mean and maximum standardized uptake values (SUVmean and SUVmax) were also recorded for selected lesions, using the software provided by the vendor. The combined metabolic information of PET and the structural and morphological information of CT were used for image interpretation. Transaxial slices of the patients showing the symmetric or asymmetric tracer accumulation in nasopharyngeal areas were chosen for region of interest analysis. Concordant metabolic-structural findings were recorded in detail. Samples of nasopharyngeal cancer, nasopharyngeal holding of Hodgkin's lymphoma, nasopharyngeal holding of T cell lymphoma, verrucous lesions of the nasopharynx, and physiological uptake are given in Figure 1.

Statistical Analysis

All data were analyzed with the Statistical Package for Social Sciences software version 21.0 (SPSS, IBM Corp, Armonk, NY, U.S.A). Distributions of normality for ordinal data were examined by the Shapiro-Wilk test. The relationship between biopsy results, visible lesions on endoscopy, and sites of uptake were evaluated by the Fisher's Exact and Chi-square tests. SUVmax was tested by the Kruskal–Wallis analysis of variance. SUVmax values for benign and malignant groups were compared by the Mann-Whitney U test. A p-value of less than 0.05 was accepted as statistically significant.

Table 1. Classification of primary malignancies

Malignant	**n**
Hodgkin lymphoma	9
Non-Hodgkin lymphoma	7
Laryngeal SCC	3
Breast invasive ductal carcinoma	1
Ovarian serous carcinoma	1
Gastric adenocarcinoma	1
Renal cell carcinoma	1
Multiple myeloma	1
Glioblastoma	1
Langerhans cell histiocytosis	1
Lung SCC	1

SCC: Squamous cell carcinoma

RESULTS

A total of 27 patients (14 men and 13 women) were analyzed in this study. The mean patient age was 53.63±20.76 years. The primary malignancies of the patients are shown in Table 1. No patients had serous otitis media or fluid accumulation in the middle ear.

When the biopsy reports were examined, 23 benign and 4 malignant results were obtained. All the malignant patients had a previous history of lymphoma (Table 2).

Three patients who had a positive nasopharynx biopsy also had diffuse large B-cell lymphoma and one patient had Hodgkin's lymphoma. The malignant biopsy results were compatible with the primary diseases. These results depicted an increased stage of the primary disease, progressing to stage III or IV.

There were 10 patients who had visible lesions in their endoscopic examinations, 6 of whom had a benign biopsy result and 4 who had a malignant result. The relationship between the visible lesions and the biopsy results was significant ($p<0.05$) (Table 3).

SUVmax values were examined in PET scans and the mean SUV-

Table 2. Nasopharynx biopsy results

Pathology	n	Mean SUVmax	Mean SUVmean
Chronic inflammation	9	6.84	3.27
Normal nasopharynx mucosa	7	6.83	3.41
Non-Hodgkin lymphoma	3	7.2	3.33
Lymphoid hyperplasia	3	8.4	4.17
Necrotisan granulomatous inflammation	2	13.85	7.45
Hodgkin lymphoma	1	12	5.5
Follicular hyperplasia	1	7.9	4.3
Verrucous hyperplasia	1	6	2.8

SUV: Standardized uptake values

Table 3. Comparison of benign and malignant biopsy results in terms of visible lesion and mean SUVmax values

	Benign pathology	Malignant pathology	p
Visible lesion/yes	6	4	0.012
Visible lesion/no	17	0	
Mean SUVmax	7.66±0.94	8.4±3.2	0.974
Mean SUVmean	3.81	3.87	0.87
Total (n)	23	4	

SUV: Standardized uptake values

max was 7.83. The highest value for SUVmax was 22.5 and the biopsy result was a chronically active necrotizing inflammatory event. When SUVmax was examined in terms of biopsy results, the mean SUVmax values were 7.66±0.94 and 8.4±3.2 for benign and malignant pathology, respectively. There was no significant difference between the SUVmax value and the benign or malignant biopsy results ($p>0.05$) (Table 3).

When median SUVmax values of lymphoma and non-lymphoma groups were compared, the median SUVmax was higher in the lymphoma group, but this difference was not statistically significant ($p=0.089$).

SUVmean values were also compared statistically. Their comparisons were similar to SUVmax results and there was no significant statistical difference ($p>0.05$).

When the relationship between the uptake type and the biopsy results were examined, there were 11 patients with symmetrical uptake and 16 patients with asymmetrical uptake in the PET scan. All patients who statistically had malignant biopsy results also had asymmetrical uptakes ($p<0.05$).

DISCUSSION

FDG PET has become a very important tool for the preliminary first staging and in defining the treatment response and recurrence of the tumor in later years (5, 6). The basic working principle of this imaging method is that glucose is used up in higher quantities in metabolically active tissues, especially in malignant tissues (7). Tissues that retain radio-labeled glucose to a greater degree are suspicious for inflammation, hyperactivity, and malignancy. There is no clear data on what kind of uptake is physiologically normal. Although there are opinions that symmetrical involvement is normal, this type of uptake could also be seen in malignant diseases. For this reason, incidental FDG uptake in PET scans that are performed for another reason lead to stress in patients and clinicians (3). Nasopharyngeal uptake can be seen in PET scans. Therein lies the question: is a biopsy necessary for all patients? Performing biopsies in all patients is not only painful, but also costly.

There are some reports on incidental FDG uptake in PET scans. Stangierski et al. reported that incidental thyroid uptake indicates a risk of malignancy and histopathological examination must be done for these patients (8). Treglia et al. mentioned that the focal FDG uptake in the colorectal area cannot be ignored and SUVmax value is not a reliable defining malignant character of the lesions (9).

Heusner et al. (3) performed a study including 590 oncological patients with incidental head and neck uptake. They retrospectively followed these patients for at least 12 months (mean: 29.5 months) without pathological confirmation. Only 2 patients were found to have developed malignancy in the follow-up. They found that biopsy is not necessary for incidental head and neck involvement, as long as there is no prominent and visible lesion. In addition, they also mentioned that biopsy is not necessary with incidental thyroid uptake in areas with endemic goiter. The difference between this study and their study is that, in the present study, there was pathologic confirmation for all patients. There were 46 patients with lymphoma in Heusner's study and incidental uptake was not significant. There were 4 lymphoma patients in our study group with nasopharyngeal involvement. Therefore, we recommended pathologic confirmation for the lymphoma patients to try a different method from Heusner's.

The uptake of radio-labeled glucose in physiologically active tissues, such as the central nervous system, myocardium, urinary system, stomach, and cecum was as expected. Additionally, lower uptake was seen in liver, lung, and skeletal muscle. There was also glucose uptake in the breast tissue and ovarian cysts periodically, as well as in the thymus, tonsils, and adenoids, depending on the patients' age. Glucose uptake could also be seen in benign diseases such as Paget's disease, hyperplastic bone marrow, and Graves' disease, and also in inflammatory conditions, such as sarcoidosis, histoplasmosis, tuberculosis, and wound healing (10). Clinical confirmation or another imaging method is recommended to confirm an underlying malignancy.

There were some mistakes and artifacts in the assessment of the head and neck area in the PET scans. The most common mistake in this area was related to the physiological uptake. FDG uptake could be seen in the Waldeyer's ring, salivary glands, skeletal muscles, and brown fat tissue. Furthermore, increased uptake could be observed in conditions such as inflammation, infection, previous surgery, chemoradiotherapy, and in the contralateral side in peripheral facial paralysis. Artifacts may also be caused by metallic and dental implants (11).

Basu et al. reported that symmetrical and bilateral uptake in parotitis was not significant. They also mentioned that asymmetrical and focal involvement must be examined carefully (12). Patel et al. re-

ported that incidental head and neck FDG uptake is not significant in patients who have non-small cell lung cancer (13).

In a 177-patient study done with the exclusion of lymphoma and nasopharynx cancer, Lee et al. reported that incidental uptake in the nasopharynx may not be related to malignancy (2). However, there were only 3 patients who received a nasopharyngeal biopsy. The other 174 patients were followed for at least 1 year. Heusner et al. examined incidental head and neck uptake, but they did not also perform biopsies on their patients (3). Al-Hakami et al. recommended that patients with incidentally detected FDG-PET-positive head and neck lesions should be evaluated with a high degree of clinical suspicion (14).

Although SUVmax values are more commonly used in clinical practice, SUVmean values are also important to determine the characteristics of the lesion. SUVmean demonstrates the average intensity uptake of the lesion. Therefore, it provides a more general perspective (15). However, there were no statistically significant differences in terms of the mean SUVmean.

In this study, all the patients who had incidental nasopharynx involvement also had a history of lymphoma. When a patient with Non-Hodgkin's or Hodgkin's lymphoma shows neoplastic proliferation in tissues different from native lymph nodes, it is called extranodal lymphoma. These diseases are considered to be at stage III or IV. This is also a prognostic factor and changes the treatment regimen (16). Due to this, even if the primary disease for incidental uptake is lymphoma, a biopsy should be considered.

In this study, biopsies were done for 27 patients who had incidental nasopharyngeal uptake. There were 4 malignant specimens. There was a significant difference between the visible lesions and the biopsy results. There was no significant relationship between malignancy and SUVmax. On the other hand, all patients who had a malignant biopsy result also had asymmetrical uptakes and lymphoma histories. The strongest aspect of this study was the comparison of the uptake type, the SUVmax values, and the biopsy results. Thus, this study confirmed the PET uptake type and the histopathological diagnosis.

CONCLUSION

In patients with incidental nasopharyngeal uptake in PET scans, a biopsy decision must be made according to the physical examination, the nature of the primary disease, and the site of involvement. A biopsy must be done in patients with a visible lesion, history of lymphoma, and asymmetrical nasopharyngeal uptake according to the PET scan. SUVmax and SUVmean values are not helpful in taking a decision whether to perform a biopsy or not.

Ethics Committee Approval: Erciyes University, Ethical Committee of Clinical Researchs (2014/358) was obtained and obeyed the guidelines of the Declaration of Helsinki.

Peer-review: Externally peer-reviewed.

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